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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LUM, LEON YUN BON

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/084,632

Applicant(s)

STARZL ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 and 33-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 33-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>2/26/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed February 6, 2006 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

2. Claims 1-19 and 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
3. Claim 1 recites the limitation "said processing step using digital information to detect the presence of said particles" in lines 12-13. There is insufficient antecedent basis for this limitation in the claim. The claimed "processing" step in lines 10-11 only includes the limitation of processing digital image data. The step does not include any limitation that applies the processed data towards detecting the presence of particles.
4. Claim 16 recites the limitation "test area" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4, 6-8, 18-19, and 36-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Yguerabide et al (US 6,214,560 B1).

Yguerabide et al reference teaches the step of selecting apparatus components (i.e. establishing a setting and a position for an instrument) by defining sample chambers (i.e. sample assay area), detection means (i.e. light collection device), and optical and electrical components in the apparatus illuminate different microspots of an array at different times (i.e. control; positioning the sample in said sample assay area relative to a light source that outputs a light beam; at a desired angle; test spot). See Figure 25, Block III; and column 85, lines 30-46. In addition, Yguerabide et al teach the steps of detecting scattered light (i.e. collecting scattered light), processing the scattered light by performing digital image analysis (i.e. processing digital image data based on said light collected), and counting the number of particles per unit area (i.e. counting individual analyte particles after said processing step). See column 9, lines

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18-23; column 9, line 52 to column 10, line 11; column 55, lines 14-20; and column 56, lines 18-26.

With respect to claim 2, Yguerabide et al teach the step of determining which microscope objective lens to use for different measurement areas (i.e. providing magnification). See column 56, lines 4-11.

With respect to claim 3, Yguerabide et al teach that optical filters can be applied (i.e. locating an optical subsystem in a direction relative to the sample). See column 53, lines 40-42.

With respect to claims 4 and 6-7, Yguerabide et al teach that the light source can be a laser (i.e. laser beam), wherein the mean angle θ can be adjusted (i.e. desired angle), and also teach the step of manually scanning each spot through the beam, wherein the beam illuminates a single microspot (i.e. beam encompass at least all of said test spot with uniform light intensity; moving at least one of the sample and said light beam). See column 60, lines 10-25; and column 82, lines 55-62.

With respect to claims 18 and 36, Yguerabide et al teach spatially addressable sites including 2-dimensional arrays. See column 86, lines 1-4.

With respect to claim 19, Yguerabide et al teach particles of different materials, including polystyrene, gold, and silver. See Table 1.

With respect to claim 37, since Yguerabide et al teach that light scattering from different microspots are detected at different times, the detection signals would necessarily be discrete signals that correspond to difference detection areas.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5, 9-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al (US 6,214,560 B1) in view of De Brabander (The Amer. J. Anat., 1989, vol. 185, pages 282-295).

Yguerabide et al reference has been disclosed above and additionally teach a CCD photodetector and both hardware and software to process information obtained by the photodetector (i.e. photoelectric device). However, Yguerabide et al fail to teach that said establishing step includes regulating a gain related to said photoelectric device to provide desired light contrast, and also fail to teach the step of adjusting a gain associated with said light collection device after conducting at least some of said processing step.

De Brabander et al reference discloses the step of subtracting an equal amount of light from all pixels (increasing the offset) and expanding the remaining signal to the original value (increasing the gain), wherein a "mottle" image obtained with the preparation out of focus is stored in digital format in a frame memory and subtracted in real time from subsequent images, in order to produce an increase in intensity (contrast) to distinguish between gold particle markers and background signal, and increase the contrast of other elements that disturb the image, and to also improve visualization of contrast generated by the preparation itself. See page 282, right column, 3rd paragraph to page 283, left column; and Figure 2 and caption.

It would have been obvious at the time of the invention to modify the method of Yguerabide et al with the step of subtracting an equal amount of light from all pixels (increasing the offset) and expanding the remaining signal to the original value

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(increasing the gain), wherein a "mottle" image obtained with the preparation out of focus is stored in digital format in a frame memory and subtracted in real time from subsequent images, as taught by De Brabander, in order to produce an increase in intensity (contrast) to distinguish between gold particle markers and background signal, and increase the contrast of other elements that disturb the image, and to also improve visualization of contrast generated by the preparation itself. The benefit of obtaining a more defined contrast between the particles and background, as taught by De Brabander, provides the motivation to combine the teachings of De Brabander with the method of Yguerabide et al. In addition, one of ordinary skill in the art at the time of the invention would have reasonable expectation of success in increasing the offset and gain of the image, as taught by De Brabander et al, in the method of Yguerabide et al since Yguerabide et al teach image detection of light scattering from gold particles, and the image processing performed by De Brabander et al is conducted on images derived from gold particles.

With regards to claims 9-13, De Brabander et al teach the step of first increasing the offset and then increasing the gain of pixels from an image (i.e. at least a first light intensity related procedure), as stated above, wherein gold particles of 20-40 nm diameter provide sufficient contrast as individual units (i.e. at least a first size procedure; filtering using at least one parameter related to size), and also teach a segmentation step based on pure gray-level information in a single pixel, wherein gold particles have significantly lower gray values than the background after 8-bit digitalization (i.e. threshold function related to light intensity; histogram analysis), and only gray levels

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lower than a certain threshold are retained to locate the gold pixels (i.e. providing a lower limit threshold based on histogram related information). See page 284, left column, 1st paragraph; and page 286, right column, 4th paragraph to page 288, right column, last paragraph.

11. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al (US 6,214,560 B1) in view of Ghaed et al (US 5,466,416).

Yguerabide et al reference has been disclosed above, but fails to teach the step of storing information in memory of said control related to said at least one of said setting and said position.

Ghaed et al reference teaches the step of storing commands for carrying out assays in a program, in order to run the assays under external control. See column 7, lines 17-22.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Yguerabide et al with the step of storing detection commands in a program, as taught by Ghaed et al, in order to run the assays under external control. The advantage of being able to execute an assay remotely provides the motivation to combine the step of Ghaed et al with the method of Yguerabide et al. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including the step of Ghaed et al in the method of Yguerabide et al, since Yguerabide et al teach an assay with detection methods, and

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the programming step of Ghaed et al allows an assay to be run, which includes detection steps.

12. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al (US 6,214,560 B1).

Yguerabide et al reference has been disclosed above, but fails to teach that said counting step includes counting objects from said first subspot before obtaining said image data from said second subspot.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Yguerabide et al by specifically counting analytes in one microspot before obtaining light scattering data from another microspot, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Applicants have not disclosed in the specification that the specific order of counting objects from a first subspot before obtaining image data from a second subspot is for a particular purpose or to solve a specific problem unknown in the prior art. Because Applicants have not disclosed why the claimed order is important, and the general workings of capturing light scatter and counting analytes derived from the light scatter are known in the prior art, it would have only involved routine skill in the art to chose one particular time over another to count analytes from captured light scatter data.

With respect to claim 17, Yguerabide et al teach that each microspot contains a different type of capture biomolecule such as an antibody, receptor, or nucleic acid to detect different types of analytes (i.e. said second subspot has a second sample different from the first sample). See column 81, lines 33-37.

13. Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al (US 6,214,560 B1) in view of Sheppard, Jr. et al (US 6,143,247).

Yguerabide et al reference has been disclosed above, but fails to teach that said analyte particle comprises bacteria.

Sheppard, Jr. et al reference teaches that bacteria can be detected by light scattering in affinity-binding based assays, in order to screen specific settings for cells that are disease-causing or that make toxins. See column 1, lines 9-15 and 40-45; and column 9, lines 15-23.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Yguerabide et al with bacteria, as taught by Sheppard, Jr. et al, in order to screen specific settings for cells that are disease-causing or that make toxins. The advantage of detecting potentially deadly contaminants provides motivation to combine the bacteria of Sheppard, Jr. et al with the method of Yguerabide et al. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in combining the bacteria of Sheppard, Jr. et al with the method of Yguerabide et al, since Yguerabide et al teach

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assays based on the principle of light-scattering, and the bacteria of Sheppard, Jr. et al is capable of being detected by light-scattering techniques.

14. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al (US 6,214,560 B1) in view of Sizto et al (US 5,556,764).

Yguerabide et al reference has been disclosed above, but fails to teach that the laser beam has an outside diameter approximately from 5-50 microns.

Sizto et al reference teaches that a laser spot has a diameter of about 10 microns. See column 9, lines 2-3.

It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable.

“[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation”

Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). “No invention is involved in discovering optimum ranges of a process by routine

experimentation.” Id. at 458, 105 USPQ at 236-237. The “discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the

art.” Since Applicants have not disclosed that the specific limitation of 5-50 microns are for any particular purpose or to solve any stated problem, and the prior art teaches that

a laser spot can have a diameter of 10 microns absent unexpected results, it would have been obvious for one of ordinary skill in the art at the time of the invention to

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discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures known in the optical detection art.

Response to Arguments

15. Applicant's arguments with respect to claims 1-19 and 33-37 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum
Patent Examiner
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04/10/06